Statistical Center for
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MEMORANDUM

Date: December 10, 2009

To: MTN 001 Protocol Team

From: MTN 001 SDMC

RE: **MTN 001 Visit Adherence Report**

Purpose

To summarize site performance regarding study primary endpoint data collection, by site and overall, with particular attention given to: 1) Distribution of visits, as the number of days between target and actual visit dates, 2) the number of days between each wash out period; 3) Number and percentage of required procedures - study product adherence and behavior assessment; last three doses of study product; acceptability assessments; final acceptability assessment; pharmacokinetic measures for intensive and non-intensive blood draws and genital specimen tests; pregnancy tests; pelvic exams; HIV tests; Safety Lab tests (including hemogram and chemistries); and product sharing assessment.

Expectations and Data Used in this Report

The measures above can only be accurately assessed if the relevant forms are expected to have been collected in the database, and have actually been received. For purposes of this report, forms are expected for visits for which the allowable window has passed. Participant visits are required and expected only if the participant comes in for a visit. Missed visits are not considered expected for purposes of this report.

Table Descriptions

Distribution of Visits: Number of Days Between Target and Actual Visit Date

For each of the visits in follow-up, we subtract the actual visit date from the target visit date among visits that were expected and completed (missed visits are not considered). The table provides the following statistics which describe the distribution of the time between target and actual visit date: 1) “N”, which is the number of participant-visits being summarized; 2) “Mean”, which is the average, a mean *greater* than 0 indicates the actual visit occurred *after* the target date, on average, and a mean *less* than 0 indicates the actual visit occurred *before* the target date, on average; 3) “STD”, which is the standard deviation; 4) “Max”, which is the maximum or the highest value; 5) “75th %tile”, which is the third quartile ; 6) “Median”, which is the median, or middle value of the distribution; 7) “25th%tile”, which is the first quartile; and 8) “Min”, which is the minimum or the lowest value.

Distribution of Visits: Number of Days Between Each Wash Out Period

For participants with end of study period visits and the next start of study period visits, we summarize the table by subtracting the visit date for the end of study period visit from the visit date of the start of the next study period visit, among visits that were expected and completed (missed visits are not considered). The table provides the following statistics which describe the distribution of the time during each of the washout periods: 1) “N”, which is the number of participant-visits being summarized; 2) “Mean”, which is the average; 3) “STD”, which is the standard deviation; 4) “Max”, which is the maximum or the highest value; 5) “75th%tile”, which is the third

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quartile; 6) “Median”, which is the median, or middle value of the distribution; 7) “25th%tile”, which is the first quartile; and 8) “Min.”, which is the minimum or the lowest value.

Completion of Procedures: (Study Product Adherence and Behavior Assessment; Last Three Doses of Study Product; Acceptability Assessment; Final Acceptability Assessment; Intensive and Non-Intensive Pharmacokinetics Blood and Genital Specimen Tests; Pregnancy Tests; Pelvic exams; HIV tests; Safety Labs - including hemogram and chemistries; and Product Sharing Assessment)

Each of the measures in this table has separate requirements regarding the visits at which the procedures are required, and the data elements on the Case Report Form (CRF) that must be received in order for the procedure to be considered “completed.” This study has procedures that need to be completed at start-, mid- and end of study period visits which are defined as follows: Start of study period visits (enrollment, weeks 7 and 14); Mid-study period visits (weeks 3, 10 and 17); end of study period visits (weeks 6, 13 and 20). In addition, there is a study exit visit scheduled to occur at week 21.

Study Product Adherence and Behavior Assessments (SPA) are required at all mid- and end of study period visits only if study product was dispensed at or after the previous reguarly scheduled visit the participant completed. An assessment is considered “Completed” if Q4 on the SPA CRF has a response.

The date and time of the last three doses of study product are required and expected at all mid- and end of study period visits, except when a participant is on a product hold/permanent discontinuation, is HIV positive, Hepatitis B reactive, pregnant or early terminated. This data element is considered “Completed” if all three required date and time fields in Q2 and/or Q3 (depending on whether corresponding study period is oral, vaginal, or dual) of the SPA CRF are completed. If at least one required date or time is missing at a given visit, this data element is considered “Partially Completed”. If no required date or time is recorded in Q2 and/or Q3 for a given visit, this data element is considered “Not Completed”.

Acceptability Assessments (AA) are required for participants at the end of study period visits for study period 1 and study period 2 only if the pariticipant used atleast one dose of study product during the given study period, as documented in items 2 and/or 3 on the SPA form. An assessment is considered “Completed” if the “current study regimen” Q1 on AA CRF is completed.

Final acceptability assessments (FAA) are required at the end of study period 3 for participants who used atleast one dose of study product during the given study period as documented in items 2 and/or 3 on the SPA form. An assessment is considered “Completed” if the “current study regimen” Q1 on FAA CRF is completed.

Pharmacokinetic (PK) measures for all participants are required at two types of visits: mid-study period and end of study period, with the exceptions of the following: participant is HIV positive, Pregnant, Hepatitis B reactive, early terminated, on product hold or permanently discontinues product use. These measures encompass the mid-study period PK blood draw, end of study period Pre- and Post-dose blood draws, and end of study period collection of Genital specimens.

A PK blood draw is required and expected for all participants at each mid-study period visit. This procedure is considered “Completed” if the sampling time for “PK blood draw” is recorded on the Pharmacokinetics Intensive (PKI) or Pharmacokinetics Non-Intensive (PKN) CRF.

Non-intensive participants are assigned to a sampling window based on their randomization to study regimen. A Pre-Dose blood draw and a Post-dose blood draw are required and expected for non-intensive participants at each end of study period visit. These procedures are considered “Completed” if the sampling times are recorded on the PKN form for both the pre-dose and post-dose blood draws. If the sampling time is missing for at least one required PK blood draw at a given end of study period visit, the procedures are considered “Partially Completed”. If the sampling time is missing for both required PK blood draws at a given end of study period visit, the procedures are considered “Not Completed”.

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PK CVL collection for non-intensive participants is required and expected at each end of study period visit. This procedure is considered "Completed" if the sampling time for PK CVL is recorded on the PKN CRF.

Intensive PK measures for all participants are required and expected at end of study period visits. The Pre-Dose blood draw and Post-dose blood draws required at each end of study period visit are considered "Completed" if the sampling times for each of the draws are recorded on the PKI CRF. If the sampling time is missing for at least one required PK blood draw at a given end of study period visit, the procedures are considered "Partially Completed". If the sampling time is missing for all required PK blood draws at a given end of study period visit, the procedures are considered "Not Completed".

PK genital specimen collection (CVL, cervical cytology brush, and vaginal tissue biopsy) for intensive PK participants is required and expected at each end of study period visit. These procedures are considered "Completed" if the sampling times for each of the genital specimens are recorded on the PKI form. If the sampling time is missing for at least one required genital specimen at a given end of study period visit, the procedures are considered "Partially Completed". If the sampling time is missing for all genital specimens at a given end of study period visit, the procedures are considered "Not Completed".

PK rectal specimen collection for intensive PK participants (Bronx Site only) is required and expected at each end-of-study period visit for participants who have consented to this procedure. Specimen collection is considered "Completed" if a collection time is recorded on the Rectal PK (RPK) form.

Pregnancy tests are required of all participants at all scheduled visits, and additionally during interim visits that occur following a missed visit. A pregnancy test is considered "Completed" if the "negative" or "positive" box is marked for the "hCG for pregnancy" item on the Follow-up Visit or Interim Visit CRF completed for the visit.

Pelvic exams are required at all mid-, and end of study period visits for all participants, and additionally at the start of the study period 2 and study period 3 visits. A pelvic exam is considered "Completed" if the item 1 "abnormal findings" or "no abnormal findings" box is marked on the Follow-up Pelvic Exam CRF completed for the visit.

HIV tests are required of all participants at the start of the study period 2 and study period 3 visits, and at study exit. An HIV test is considered "Completed" if the "negative" or "positive" box is marked for the Rapid Test or ELISA item on the STI Laboratory Results CRF completed for the visit. HIV tests are not required for participants who are confirmed HIV-infected during study follow-up.

Safety laboratory results, which include the hemogram tests and chemistries for liver and renal function tests as listed in Appendix I of the protocol, are required of all participants. Hemogram tests are required at the start of study periods 2 and 3 (the Week 7 and 14 Visits). Blood chemistries are required at all scheduled visits and at study exit. Safety labs are considered "Completed" when SCHARP has received a Safety Laboratory Results CRF with a value for each test. The table reports separately the number of participant-visits with "Hemogram" lab tests completed, and the number of participant-visits with "Chemistries" lab tests completed.

Product sharing assessments (PSA) are required at 6-week (end of study period 1) visits for all participants. These assessments are required at 13-week (end of study period 2) and 20-week (end of study period 3) study visits only if the participant was dispensed study product at any time during that period. An assessment is considered "Completed" if Q1 on the PSA CRF is completed.

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